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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/282,239 | 03/31/1999 | STEVEN A. GOLDMAN | 19603/1426 | 8339 |

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| EXAMINER | |
|---|---|
| HUTSON, RICHARD G | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/282,239 | GOLDMAN ET AL. | |
| | Examiner | Art Unit | |
| | Richard G. Hutson | 1652 | |

*-- The MAILING DATE of this communication app ars on the cov r she t with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *25,26 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Und r 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/25/2004 has been entered.

Applicants amendment the specification and of claims 25, 26 and 29 in the paper of 10/25/2004, is acknowledged. Claims 25, 26 and 29 are at issue and are present for examination.

Applicants' arguments filed on 10/25/2004, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### *Specification*

The disclosure is objected to because of the following informalities:

Applicants amendment in response to the previous objection to the specification is acknowledged, however, applicants have not pointed out where in the specification support for this amendment may be found. Since such support is not obvious this amendment of the specification which on page 11, line 4,

which recites "an oligodendrocyte progenitor and a JC virus minimal core promoter (Krebs et al. 1995)" is objected to as containing new matter.

Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 25, 26 and 29 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Rao et al. (U.S. Patent No. 6,361,996 B1).

The rejection is stated in the previous office action as it applied to previous claims 25, 26 and 29. In response to this rejection applicants have amended claims 25, 26 and 29 and traverse the rejection as it applies to the newly amended claims.

For applicants convenience the previous rejection is repeated herein. Rao et al. teach an isolated, pure and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are capable of self-renewal and

differentiation into oligodendrocytes and astrocytes and methods of generating, isolating and culturing such oligodendrocyte-astrocyte precursor cells. The specific pure homogeneous population of cells isolated by Rao et al. is illustrated in Figure 1 (See specifically cell type –14, and the supporting text) and while applicants specifically teach as an example said pure homogeneous preparation of cells as isolated from rat, applicants point out that the invention encompasses all mammalian neuroepithelial stem cells and is not limited to neuroepithelial stem cells from the rat. Mammalian neuroepithelial stem cells can be isolated from human and non-human primates, equines, canines, felines, bovines, porcines, ovines, lagomorphs, and the like. Thus, Rao et al. anticipates a claim to a enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, wherein an oligodendrocyte specific promoter functions in all cells of the enriched or purified preparation.

Claims 25 and 26 which are drawn to the preparation of oligodendrocyte progenitor cells of claim 29 are included in this rejection because these product-by-process like limitations do not change the oligodendrocyte progenitor cells of claim 29. Rao further teach that a better understanding of a number of tumors and other diseases in humans could be facilitated by a better understanding of these cell types and the ability to isolate and grow these mammalian cells in vitro, which allows for the possibility of using such stem cells to treat neurological disorders in mammals, particularly humans. Further, such mammalian neuroepithelial stem cells can be used therapeutically for treatment of certain diseases, e.g. Parkinson's Disease, such as by transplantation of such cells into

an afflicted individual. Moreover, such cells can still further be used for the discovery of genes and drugs that are useful for treating certain of these diseases.

One of ordinary skill in the art at the time of filing would have been motivated to use the methods taught by Rao et al. to isolate an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells from humans so that these pure cell preparations could be used to treat neurological disorders in humans, such as. Parkinson's Disease, such as by transplantation of such cells into an afflicted individual. This motivation is suggested by Rao et al. and the reasonable expectation of success comes from the results of Rao et al. who successfully isolated such an enriched or purified preparation of mitotic oligodendrocyte progenitor cells from rat.

The rejection is stated in the previous office action as it applied to previous claims 25, 26 and 29. In response to this rejection applicants have amended claims 25, 26 and 29 and traverse the rejection as it applies to the newly amended claims. It is noted that applicants amendment which recites "oligodendrocyte-specified progenitor cells" is interpreted as "oligodendrocyte-restricted progenitor cells", that is a progenitor cell population which develops oligodendrocytre cells exclusively.

Applicants newly submitted arguments based on/and the declaration by Dr, Mahendra S. Rao are fully acknowledged.

Applicants continue to submit that Rao et al. discloses multipotential neuroepithelial stem cells and that these cells are characterized as

"multipotential intermediate precursor cells restricted to glial lineages" and that since Rao's astrocyte/oligodendrocyte precursor cells are not committed to formation of oligodendrocytes and therefore are in a less differentiated state than the claimed oligodendrocyte progenitor cells, it is apparent that this reference in no way suggests the claimed invention, which applicants have now amended to "oligodendrocyt-specified progenitor cells".

Applicants argument is not found persuasive because applicants continued submission of the differences between the cells taught by Rao and the cells taught in the instant application as isolated from human are acknowledged and understood, however, applicant is reminded that applicants invention as disclosed by applicants specification and applicants invention as encompassed by the rejected claims are not necessarily the same invention and that applicants should direct their arguments to the rejected claims, not applicants specification. As discussed above and previously, applicants claimed invention is anticipated by or, in the alternative, obvious over Rao et al. Applicants appear to be arguing that based on the above using the teachings of Rao one If skill in the art would not have a reasonable expectation of success in achieving the oligodendrocyte-specified progenitor cell preparation as taught by the instant specification because the cells of Rao are in a less differentiated state then that of the instant invention. While this may be true, it remains to be seen that the cell preparation taught by Rao continues to anticipate an enriched or purified preparation of human mitotic oligodendrocyte-specified progenitor cells including those wherein the cells are derived from a post-natal or an adult human, (see above comments

to product-by process issues), wherein a human cyclic nucleotide phosphodiesterase 2 promoter is transcriptionally active in all cells of the enriched or purified preparation. The preparation taught by Rao is such that a human cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the enriched or purified preparation. This is evidenced by the reference Scherer et al. (Neuron Vol 12, pp 1363-1375, June 1994, see applicants IDS) who teach the differential cellular and temporal regulation of the 2',3'-cyclic nucleotide 3'-phosphodiesterase gene (CNP)and teach that the 2',3'-cyclic nucleotide 3'-phosphodiesterase II promoter is transcriptionally active in oligodendrocytes, Schwann cells and many additional tissues and appears before the appearance of mature oligodendrocytes, in oligodendrocyte precursor cells early in brain development (See page1365-1367, Figures 4 and 5 and supporting text). It is noted that applicants have not addressed this point of the transcriptional activity of the 2',3'-cyclic nucleotide 3'-phosphodiesterase II promoter in cells other then oligodendrocytes.

Applicants further continue to submit that in addition to the above, Rao also worked with cells from rats rather than from humans, as required by the claimed invention and that for the same reasons pointed out in the June 10, 2002 preliminary amendment based on the "First Goldman Declaration" the teachings of Rao are not pertinent to the claimed invention, although it is noted that the referred to declaration was directed to U.S. patent No. 5,276,145 to Bottenstein, applicants representative notes the issues are substantially the same. Applicants continue to point out that there are fundamental differences between the biology

of rat and human oligodendrocyte progenitor cells as well as fundamental differences between the lineage restriction and potential of neonatal and adult oligodendrocyte progenitor cells ("Third Goldman Declaration"). Applicants note that these biological differences pointed out above and in the supporting declarations were not recognized by either Rao or Bottenstein. Based on the above applicants submit that rat oligodendrocyte progenitor cells cannot be considered homologous to its human counterparts and methods that are used for the selective extraction of rat oligodendrocyte progenitor cells do not differentiate between oligodendrocyte progenitor cells and mature oligodendrocytes able to reenter the mitotic cycle.

Applicants further submit that rat oligodendrocyte progenitors and oligodendrocytes both express the antigenic marker recognized by monoclonal antibody O4 (Third Goldman Declaration), but applicants note that this marker is not expressed by mitotic (human) oligodendrocyte progenitor cells., thus a method of separation of these two types of cells in human can not be based on the use of O4 selection.

Applicants finally conclude from above and the supporting declarations, that thus the selective propagation of mitotically active oligodendrocyte progenitor cells from neonatal rat brain, as taught by Rao does not predict the successful isolation of mitotic oligodendrocyte-specified progenitor cells from postnatal or adult human brain tissue.

As discussed above, applicants submission of the differences between the cells taught by Rao and the cells taught in the instant application as isolated from

human are acknowledged and understood, however, applicant is reminded that applicants invention as disclosed by applicants specification and applicants invention as encompassed by the rejected claims are not necessarily the same invention and that applicants should direct their arguments to the rejected claims, not applicants specification. As discussed above and previously, applicants claimed invention is anticipated by or, in the alternative, obvious over Rao et al. Applicants continue to argue that based on the above using the teachings of Rao one If skill in the art would not have a reasonable expectation of success in achieving the oligodendrocyte-specified progenitor cell preparation as taught by the instant specification because the cells of Rao are in a less differentiated state then that of the instant invention. While this may be true, it remains to be seen that the cell preparation taught by Rao continues to anticipate an enriched or purified preparation of human mitotic oligodendrocyte-specified progenitor cells including those wherein the cells are derived from a post-natal or an adult human, (see above comments to product-by process issues), wherein cyclic nucleotide phosphodiesterase 2 promoter is transcriptionally active in all cells of the enriched or purified preparation. As discussed above, the preparation taught by Rao is such that a cyclic nucleotide phosphodiesterase 2 promoter is transcriptionally active in all cells of the enriched or purified preparation inherently and applicants in their response have not addressed this point.

Applicants like the above and previous arguments further continue to argue the differences between the cell population taught by Rao et al. and that taught by the instant specification on the basis that adult cells as taught by the

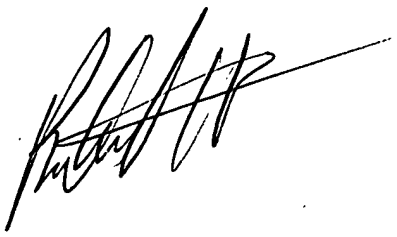
instant application produce myelin much more quickly. This complete argument is acknowledged, as the above and previous arguments, but found non-persuasive for the same reasons discussed above, that the difference between that cell population taught by Rao et al. and that cell population taught by the instant specification are not necessarily relevant to that cell population claimed. It is that cell population claimed that remains rejected for the reasons stated above and previously.

As discussed previously and above, Rao et al. teach an isolated, pure and homogeneous population of lineage-restricted oligodendrocyte-astrocyte precursor cells which are capable of self-renewal and differentiation into oligodendrocytes and astrocytes and based on the above evidence, the cyclic nucleotide phosphodiesterase 2 promoter is inherently transcriptionally active in all cells of the enriched or purified preparation. While applicants specifically teach as an example said pure homogeneous preparation of cells as isolated from rat, applicants point out that the invention encompasses all mammalian neuroepithelial stem cells including those isolated from human and non-human action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
12/28/2004